

509,090

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
9 October 2003 (09.10.2003)

PCT

(10) International Publication Number  
**WO 03/082361 A2**

(51) International Patent Classification<sup>7</sup>: **A61L 27/00**

(21) International Application Number: PCT/GB03/01368

(22) International Filing Date: 28 March 2003 (28.03.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0207416.9 28 March 2002 (28.03.2002) GB

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(74) Agents: PAGET, Hugh, C.E. et al.; Mewburn Ellis, York House, 23 Kingsway, London, Greater London WC2B 6HP (GB).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Alphabetic Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 03/082361 A2

(54) Title: DELIVERY ASSEMBLY FOR USE IN SURGERY

(57) Abstract: A delivery assembly for use in surgery particularly laparoscopic surgery, comprises a surgically implantable construct (1) containing viable cells, a support (2) on which the construct is removably carried and holding means such as a vacuum system (4, 5) releasably holding the construct on the support. The support (2) is selected from a tube having an interior surface on which the construct is held, and a rod having an exterior surface on which the construct is held. The support protects the delicate construct and maintains it in a desired position for surgical manipulation.

DELIVERY ASSEMBLY FOR USE IN SURGERYFIELD OF THE INVENTION

This invention relates to a delivery assembly for  
5 use in surgery, which is applicable in any surgical  
technique practised on a human or animal body, and in  
particular in robot-controlled laparoscopic techniques.

BACKGROUND OF THE INVENTION

Many surgical techniques involve the implantation  
10 of a surgically implantable construct, for example a  
replacement blood vessel in coronary artery bypass  
surgery. Instead of the large-scale opening of the  
patient's chest to perform heart surgery, laparoscopic  
15 techniques have been used recently in which one or more  
small apertures are opened, and surgery is carried out by  
means of instruments controlled remotely by the surgeon,  
together with an observation device such as an endoscope.  
More recently, robotic procedures have been put into  
20 practice in laparoscopic surgery, in which the  
instruments inside the patient's body are not directly  
manipulated by the surgeon but are controlled by a  
computer-operated robotic apparatus which also may  
present a visual image of the operation site to the  
25 surgeon, for example the techniques developed by the  
companies Intuitive Surgical (known as Da Vinci) and  
Computer Motion.

In such laparoscopic techniques, it is necessary  
to deliver a surgically implantable construct containing  
viable cells to the implantation site, and manipulate it  
30 there. Hitherto this has been done by means of a  
surgical tool or tools having tweezer-like grippers. An  
implant construct such as a replacement blood vessel,

which may be a blood vessel derived from the patient's own body or may be an artificial construct, is delicate and liable to damage. Its positioning in the body during its implantation, e.g. by suturing, requires care.

5      SUMMARY OF THE INVENTION

The present inventors have noted a need for an improved delivery system for a delicate surgically implantable construct, particularly in laparoscopic surgery, for one or both of the steps of delivering the construct to the implantation site, and maintaining the construct in a desired position or positions at the site during the surgical operation.

According to the present invention there is provided a delivery assembly for use in surgery, comprising a surgically implantable construct containing viable cells, a support on which the construct is removably carried and holding means for releasably holding the construct on said support, wherein the support is selected from:

20      (i) a tube having an interior surface on which the construct is held, and

      (ii) a rod having an exterior surface on which the construct is held.

This delivery assembly provides the advantages of protection of the construct, since it is held on the holding surface of the tube or rod in a controlled manner, and of making it possible to mount the construct in a predetermined and known position on the support, which is of value particularly in a robotic technique.

30      The support can be easily moved and positioned and permits the construct to be released when desired.

Surgical steps, such as suturing, can be carried out with

the construct maintained *in situ* on the support. Techniques are available to the surgeon for suturing the construct, such as a blood vessel tube, even when it is mounted on the holding surface, such as the internal 5 surface of a support in the form of a tube.

To provide a gentle holding of the construct, and easy application of the holding force and its release, the holding means is preferably suction holding means or one or more inflatable members. Suction holding means 10 may comprise one or more apertures in the surface on which the construct is held. Such apertures can connect to a conduit or conduits within the support. The support surface may have one or more grooves connected to such an aperture or apertures. An inflatable member may form 15 part of the support surface, and is expansible by means of pressure supplied through a conduit in the support in order to grip the construct. Alternatively or additionally an inflatable member may be separate from the support, for example a balloon-like member inserted 20 within a tubular implantable construct.

The surgically implantable construct may be of natural origin, for example a blood vessel derived from the patient, or may be an artificial construct, in particular one containing viable cells which requires 25 careful handling.

By viable cells are meant cells which are living or can be regarded as living since they are resuscitable.

The artificial surgically implantable construct 30 containing viable cells employed in this invention may be in the form of a sheet, tube or hollow organ and typically comprises a sheet, tube or hollow organ

containing or consisting of conjoined cells and  
extracellular matrix, together with preferably a layer of  
endothelial cells on at least one surface thereof. The  
cells joined by extracellular matrix are typically smooth  
5 muscle cells or fibroblasts. Examples are

sheet:

skin construct: sheet of fibroblasts and  
extracellular matrix (ECM), with an epithelial cell  
10 layer

hollow organ (in the form of tube):

bladder : smooth muscle/ECM tube + transitional  
epithelium  
15 stomach : smooth muscle/ECM + specialised gastric  
type epithelium

tube:

portion of gut (e.g. oesophagus, small intestine,  
20 colon, rectum):  
oesophagus - smooth muscle/ECM + squamous  
epithelium  
small intestine/colon/rectum - smooth  
muscle/ECM + columnar epithelium + goblet cells  
25 blood vessel or arterio-venous shunt : smooth  
muscle cells/ECM with endothelial cell layer  
urethra or ureter - smooth muscle/ECM +  
transitional epithelium

30 The production of artificial constructs in the  
form of sheets or tubes containing living cells, is  
described in our International Patent Application filed

on 26 March 2002 and published as WO 02/077336, and also in our co-pending UK Patent Application 0301834.8 filed 27 January 2003. The content of these patent applications is incorporated herein by reference.

5 In the construct which is to be a portion of the gut, e.g. oesophagus, stomach, small intestine, colon or rectum, the smooth muscle cell tube may desirably have a multiple layer structure, e.g. double or triple layer. A method of forming such a multiple layer is disclosed in

10 WO 02/077336.

Furthermore, the support of the delivery device of the invention may be a tube in which the artificial construct has been made in accordance with methods described in WO 02/077336.

15 To aid manipulation and positioning of the implantable construct, the support of the delivery assembly may be flexible in a manner such that it maintains a bent shape given to it. Certain plastics materials, e.g. in the form of a rod, hold a bent shape to which they are manipulated. Alternatively the support of the delivery assembly may be in the form of articulatedly connected elements, whose interconnections are adapted to maintain positions to which they are brought.

25 According to the invention there is also provided a method of surgery wherein a delivery assembly of the invention as described above is employed to bring the surgically implantable construct to its implantation site, and optionally hold it in position at said site during the performance of one or more surgical steps on it. In robotic surgery, the delivery assembly may be controlled in position by a computer controlled robotic

device. Typically, the path by which the implantable construct is brought to the implantable site is outside the arterio-venous system of the patient. At the implantation site, the construct may be sutured while still supported by the support of the delivery device.

5                   BRIEF INTRODUCTION OF THE DRAWINGS

Embodiments of the invention will now be described by way of example, with reference to the accompanying drawings, in which:-

10                  Fig. 1 is a schematic sectional view of a delivery assembly of the invention.

Fig. 2 is a schematic sectional view of the second delivery assembly according to the invention.

DESCRIPTION OF EMBODIMENTS

15                  Fig. 1 shows an implantable surgical construct in the form of a flexible tube 1 which is to be implanted as a replacement blood vessel in the patient. As mentioned above, the implant contains or consists of living cells. The tube 1 is carried on the internal cylindrical surface 20 3 of a rigid cylindrical tubular support 2. The support has a hollow wall 4 and apertures 5 opening at the internal surface, so that by application of reduced pressure inside the wall 4, the implant tube 1 is held by suction against the surface 3. A connection conduit 6 is shown, for the application of the suction pressure. As 25 shown, the implant tube 1 projects slightly from the support 2, so that its end is available for suturing at the surgical site, but this is not necessary. A typical diameter of the tube 1 is 0.5 cm.

30                  An alternative form of holding means for the implant tube 1 in the assembly of Fig. 1 is a balloon (not shown) which is inserted inside the tube 1 and

inflated to hold the tube 1 against the internal surface 3 of the support.

The support 2 can be held at its remote end (not shown) in order to be inserted into the patient through a laparoscopic aperture and can be readily manipulated, e.g. by robotic means. The holding and release of the implant tube 1 by the support is also controlled remotely.

Fig. 2 shows a second delivery assembly embodying the invention, in which the support for the surgical implant tube 1 is a hollow rigid rod 7 having apertures 5 in its surface for the application of suction pressure to hold the implant tube 1 on the external surface 8 of the rod 7. Although the implant tube 1 is exposed in this embodiment, it is nevertheless protected against kinking or other forms deformation by the supporting rod 7 and can be brought to the surgical site in a controlled manner and maintained accurately in a controlled position at the site, for example while suturing is carried out on it. Instead of the use of suction apertures for holding the implant tube 1 on the support surface 8, the rod may have one or more inflatable structures on its surface which are expanded by pressurised gas supplied along the hollow rod, to grip the implant tube 1. As in the case of the support tube of Fig. 1, the support rod is suitable to be held and controlled from the exterior of the patient's body, for example by robotic device.

**CLAIMS:**

1. Delivery assembly for use in surgery, comprising a  
surgically implantable construct containing viable cells,  
5 a support on which said construct is removably carried  
and holding means for releasably holding said construct  
on said support, wherein said support is selected from  
(i) a tube having an interior surface on which  
said construct is held, and  
10 (ii) a rod having an exterior surface on which  
said construct is held.

2. Delivery assembly according to claim 1, wherein  
said holding means is suction holding means comprising  
15 one or more apertures in said surface on which said  
construct is held.

3. Delivery assembly according to claim 1, wherein  
said holding means comprises one or more inflatable  
20 members inflatable to grip said construct.

4. Delivery assembly according to any one of claims 1  
to 3, wherein said surgically implantable construct is a  
tube.

25 5. Delivery assembly according to any one of claims 1  
to 4, wherein said surgically implantable construct is of  
natural origin.

30 6. Delivery assembly according to any one of claims 1  
to 4, wherein said surgically implantable construct is  
artificial.

7. Delivery assembly according to any one of claims 1 to 6, wherein said support is flexible and adapted to maintain a bent shape to which it is brought.

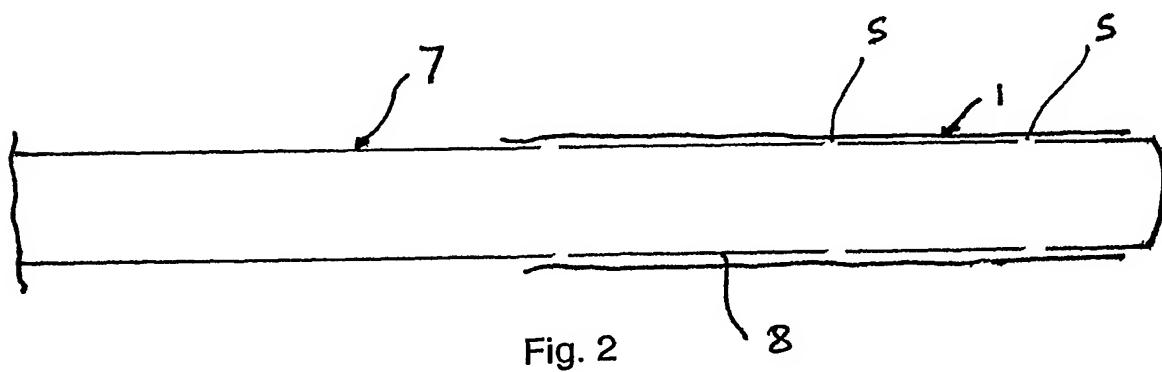
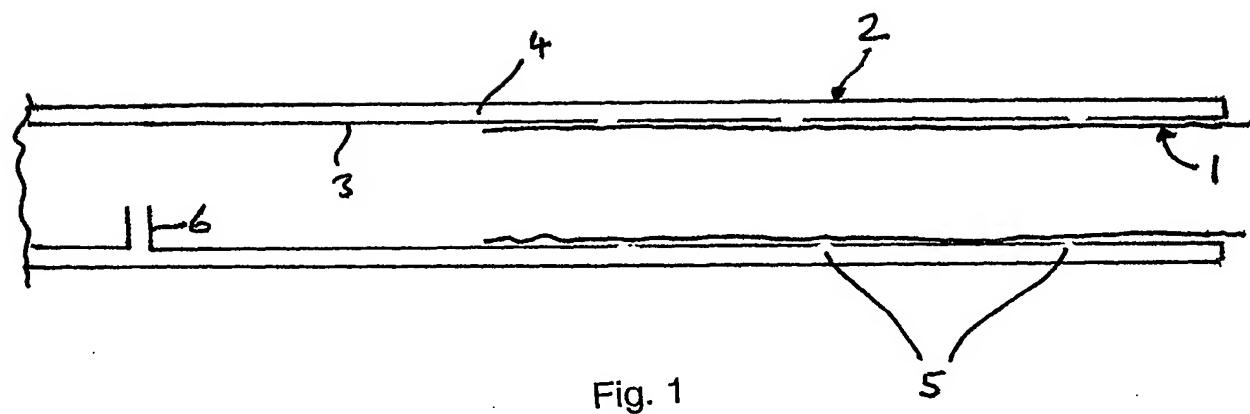
5

8. A method of surgery wherein a delivery assembly according to any one of claims 1 to 7 is employed to bring said construct to its implantation site and hold it in position at said site.

10

9. A method according to claim 8, wherein said delivery assembly is controlled in position by a computer-controlled robotic device.

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(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
9 October 2003 (09.10.2003)

PCT

(10) International Publication Number  
**WO 03/082361 A3**

(51) International Patent Classification<sup>7</sup>: **A61L 27/50**, 27/38, 31/00, A61B 19/00

(21) International Application Number: **PCT/GB03/01368**

(22) International Filing Date: 28 March 2003 (28.03.2003)

(25) Filing Language: English

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(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

(88) Date of publication of the international search report:  
18 December 2003

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

WO 03/082361 A3

(54) Title: DELIVERY ASSEMBLY FOR USE IN SURGERY

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## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB 03/01368

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 A61L27/50 A61L27/38 A61L31/00 A61B19/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A61L A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6 120 513 A (BAILEY ROBERT W ET AL) 19 September 2000 (2000-09-19) claims; figures	1-9
P, Y	WO 02 07736 A (CADILA PHARMACEUTICALS LTD ;KHAMAR BAKULESH MAFATLAL (IN)) 31 January 2002 (2002-01-31) cited in the application claims; figures	1-9
A	DE 196 00 519 A (PIER ARNOLD DIPL ING DR MED) 10 July 1997 (1997-07-10) claims; figures	1-9
A	US 5 741 274 A (KINNEY EDWARD V ET AL) 21 April 1998 (1998-04-21) claims; figures	1-9
		-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the International filing date but later than the priority date claimed

- \*T\* later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the International search

Date of mailing of the International search report

18 September 2003

30/09/2003

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB 03/01368

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 95 34244 A (DABEGRAN TECHNOLOGY INC) 21 December 1995 (1995-12-21) claims; figures -----	1-9
A	US 5 922 026 A (CHIN ALBERT K) 13 July 1999 (1999-07-13) claims; figures -----	1-9
A	EP 0 393 788 A (KOKEN KK) 24 October 1990 (1990-10-24) claims; figures -----	1-9

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 03/01368

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  
**Although claims 8-9 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.**
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

national Application No	
PCT/GB 03/01368	

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